steroids has not been evaluated in a randomized trial, their widespread use warranted mention in his review.

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1. Welch KMA. Drug therapy of migraine. N Engl J Med 1993;329:1476-83.
2. Gallagher RM. Emergency treatment of intractable migraine. Headache 1986;26:74-5.
3. Tollison CD, Kunkel RS, eds. Headache diagnosis and interdisciplinary treatment. Baltimore: Williams & Wilkins, 1993.
4. Couch JR Jr, Diamond S. Status migrainosus: causative and therapeutic aspects. Headache 1983;23:94-101.
5. Olesen J, Tfelt-Hansen P, Welch KMA, eds. The headaches. New York: Raven Press, 1993.

To the Editor: Welch suggests that ketorolac "can be used for emergency treatment of severe migraine attacks complicated by vomiting, although the drug is less effective than other parenteral antimigraine preparations." This recommendation was based on a study of patients who had no response to their usual medication.[1] Ketorolac is a nonsteroidal antiinflammatory agent that has serious side effects. In a worldwide survey, the incidence of serious side effects was 1 per 10,000 treated patients; the most common reactions were gastrointestinal disorders (22 percent), blood dyscrasias (20 percent), and renal impairment (13 percent).[2,3] As of June 1993, 97 deaths had been reported among patients given ketorolac, and marketing of the drug has been suspended in France and Germany. In our opinion the risk–benefit ratio of ketorolac is unfavorable, arguing against its use in the treatment of migraine.

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1. Klapper JA, Stanton JS. Ketorolac versus DHE and metoclopramide in the treatment of migraine headaches. Headache 1991;31:523-4.
2. Ketorolac: new restrictions on dose and duration of treatment. Curr Probl 1993;19:5-6.
3. Ketorolac tromethamine. Prescr Int 1993;2(7):104-6.

Dr. Welch replies:

To the Editor: Drs. Lahad and Friedman take me to task for not recommending corticosteroids in my review. My reasons can be explained by a critical appraisal of the same literature they quote in favor of doing so. I assume that by "prolonged migraine" they mean intractable migraine, a clinical state that is itself poorly defined. The reference they provide, apart from the textbook, is one by Gallagher,[1] who reported that among a group of patients who had headache that lasted more than 16 hours and were treated with 8 mg of dexamethasone parenterally in addition to meperidine and promethazine, 72 percent had no or mild headache when contacted 24 hours later. This was a very short report of an open study based on a retrospective chart review. The study groups had unequal numbers of patients and were not matched for age or sex, and the results were not subjected to statistical analysis. There was no measure of the severity of headache before treatment, although this was used as an outcome measure 24 hours later, and the mode of dexamethasone administration was not stated. There were also no details about the questionnaire administered over the telephone 24 hours after treatment, and it is doubtful that all the patients were questioned precisely 24 hours after treatment. Thus, the literature offers no support for the use of corticosteroids as a first- or second-line treatment for migraine. To quote Edmeads's pithy comment,[2] this treatment for migraine "must be viewed in the light of the traditional role of corticosteroids as the pharmacological last rite for neurological disease."

With respect to the use of parenteral ketorolac for a severe migraine attack, I stated that the drug "can be used for emergency treatment," and then went on to comment about its efficacy, as quoted by Drs. Mignot and Kopp. I am confident that a critical clinician would not interpret this as a recommendation. They are correct in stating that regulatory authorities in Germany and France have suspended the license for the injectable form of ketorolac pending further study. A recent post-marketing surveillance study of 20,000 patients demonstrated that "the safety profile of injectable ketorolac was no different from that seen in clinical trials which formed the basis of the approval of ketorolac for marketing."[3] An interim analysis of these data appears in the package insert for the drug in preparations purchased in the United States.

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1. Gallagher RM. Emergency treatment of intractable migraine. Headache 1986;26:74-5.
2. Edmeads J. Emergency management of headache. Headache 1988;28:675-9.
3. F.D.C. Reports. January 3, 1994:2.

TOBACCO-SPECIFIC LUNG CARCINOGEN AND EXPOSURE TO PASSIVE SMOKING

To the Editor: We think that the study by Hecht et al. (Nov. 18 issue)[1] does not provide much support for the existing weak epidemiologic evidence that passive smoking increases the risk of lung cancer. The relative risk associated with passive smoking, as calculated by the U.S. Environmental Protection Agency (EPA) in a meta-analysis of 35 studies, was about 1.4.[2] The authors propose that the tobacco-specific nitrosamines 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL) are responsible for adenocarcinomas in nonsmokers exposed to environmental tobacco smoke. Since this type of carcinoma is predominant among nonsmokers irrespective of their exposure to such smoke, NNK may not be involved in the pathogenesis of lung cancer at all. Although NNK can induce lung tumors in animals, the biologic relevance of the results reported by Hecht et al. is doubtful. The authors noted that NNK uptake is about 120 times greater in smokers than in nonsmokers experimentally exposed to sidestream cigarette smoke. According to a paper by some of the same authors,[3] NNK concentrations in smoke-polluted bars are about 10 times lower than those in the recent study.[1] As a result, the exposure-dose ratio between smokers and passive smokers is about 1200 to 1 under real-life conditions. The relative risk of lung cancer among active smokers as compared with nonsmokers is generally assumed to be somewhere between 10 and 20. If the reduction in the risk is proportional to the exposure-dose ratio, the relative risk for nonsmokers should be somewhere between 1.0075 and 1.0016. After comparing these estimates with the EPA estimate of 1.4, one can draw one of the following conclusions: the risk estimate calculated by the EPA is wrong by a factor of at least 25; NNK is not the principal lung carcinogen in smokers and nonsmokers, as claimed by

Hecht et al.; or the dose–response curve and the corresponding risk reduction deviate considerably from linearity.

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1 Hecht SS, Carmella SG, Murphy SE, Akerkar S, Brunnemann KD, Hoffmann D. A tobacco-specific lung carcinogen in the urine of men exposed to cigarette smoke. N Engl J Med 1993;329:1543–6.
2 Respiratory health effects of passive smoking: lung cancer and other disorders. Washington, D.C.: Environmental Protection Agency, 1992.
3 Brunnemann KD, Cox JE, Hoffmann D. Analysis of tobacco-specific N-nitrosamines in indoor air. Carcinogenesis 1992;13:2415–8.

The authors reply:

To the Editor: Our study demonstrated the uptake and metabolism of a tobacco-specific lung carcinogen, NNK, in nonsmokers exposed to environmental tobacco smoke. Since NNK and its metabolite NNAL are derived from nicotine, their uptake signals exposure to lung carcinogens in tobacco products.

The exposure to nicotine and NNK in our study was greater, perhaps by as much as 10 to 20 times, than in most real-life situations, as we stated in our paper. Therefore, the levels of NNAL that one would find in the urine of nonsmokers in most types of exposure would probably be less than those reported in our paper, as we also stated. Dr. Überla has attempted to calculate relative risk on the basis of these lower exposures. This is speculative and assumes a linear relation between exposure and risk. Previous studies have shown that the metabolic activation of NNK leading to promutagenic DNA adducts, which are involved in the induction of lung cancer, is dependent on dose. The efficiency of DNA alkylation increases at lower doses, resulting in higher levels of adducts than would have been expected from linear extrapolation from higher doses.[1,2]

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Sharon E. Murphy, Ph.D.
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1 Belinsky SA, White CM, Devereux TR, Swenberg JA, Anderson MW. Cell selective alkylation of DNA in rat lung following low dose exposure to the tobacco specific carcinogen 4-(*N*-methyl-*N*-nitrosamino)-1-(3-pyridyl)-1-butanone. Cancer Res 1987;47:1143–8.
2 Murphy SE, Palomino A, Hecht SS, Hoffmann D. Dose-response study of DNA and hemoglobin adduct formation by 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone in F344 rats. Cancer Res 1990;50:5446–52.

SUICIDE BY ASPHYXIATION AFTER THE PUBLICATION OF *FINAL EXIT*

To the Editor: The article by Marzuk et al. (Nov. 11 issue)* on the increase in suicide by asphyxiation in New York City after the publication of *Final Exit* confirms what many of us who keep statistics already knew. My book has not increased the number of suicides in the United States, but it has changed the method by which some people end their lives. The plastic bag is a bloodless, nonviolent method, whereas guns, knives, and jumps from high places are not.

Marzuk et al. raise the alarm that the plastic-bag method does not give a person time to reconsider suicide. But it does. It takes 30 minutes for the sealed bag to deprive the person of oxygen. If he or she has also ingested drugs, they require at least 15 minutes to work. There is no similar moratorium once the trigger has been pulled, or the jump made.

The study also raises the alarm that the plastic-bag method is being used by an undue number of depressed people, as compared with those who are terminally ill. What no survey will ever uncover is that a terminally ill person who wishes to accelerate the end of his or her life usually does so in the company of family or friends. (It is a credo of the Hemlock movement that one does not act alone if it can be avoided.) Once breathing stops, family or friends pull off the bag. Therefore, the medical examiner is unaware of the method, and the death certificate records the underlying illness as the cause of death.

A depressed person who commits suicide acts alone, of course, with no one present to destroy the evidence. If the plastic-bag method has been used, it is recorded as the cause of death.

The plastic bag is getting the same sort of public-relations reputation as the wire coat hanger did in the abortion debate, except that the bag is 100 percent effective. When are we going to get down to rethinking the laws and guidelines on the right to choose to die with the assistance of willing physicians, so that *Final Exit* can be trashed and Dr. Jack Kevorkian can go into retirement?

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The authors reply:

To the Editor: Mr. Humphry contends that the method of suicide he recommends is superior to other means because it allows people time to reconsider their actions. However, plastic bags, if small and tightly sealed, lead to suffocation in less than 30 minutes. Moreover, people who ingest the sedating drugs he recommends before applying the bag are unlikely to be in a lucid state of mind to reflect on the relative merits and disadvantages of suicide.

As Humphry suggests, the true suicide rate, an unknowable number, may be higher. Our study could not identify those people who might have had serious medical illnesses and killed themselves by asphyxiation, whose relatives then removed the plastic bag, and who were presumably certified as having died naturally. This should provide little comfort. As serious medical illnesses become more chronic, the concept of "terminal" illness is defined more broadly. Almost anyone with a chronic illness that is not imminently life-threatening will, at times, be gripped by pain, disability, or hopelessness. As compared with its lengthy advice on suicide, *Final Exit* offers little advice on how to seek relief from pain or physical discomfort or how to recognize the signs of depression.

Humphry takes pride in the fact that his recommended method of suicide is bloodless and nonviolent. But dead is dead. No amount of salesmanship about the aesthetics of this method will change either the biologic reality or the ethics of what he advocates.

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*Marzuk PM, Tardiff K, Hirsch CS, et al. Increase in suicide by asphyxiation in New York City after the publication of *Final Exit*. N Engl J Med 1993;329:1508–10.